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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/661,730	09/12/2003	Michael Philip Clark	8717MC	8312

27752 7590 03/15/2005

THE PROCTER & GAMBLE COMPANY
INTELLECTUAL PROPERTY DIVISION
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EXAMINER	
MCKENZIE, THOMAS C	
ART UNIT	**PAPER NUMBER**
1624	

DATE MAILED: 03/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/661,730	CLARK ET AL.	
	Examiner	Art Unit	
	Thomas McKenzie, Ph.D.	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/10/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to an application filed on 9/12/03. There are eight claims pending and eight under consideration. Claims 1 and 3 are compound claims. Claims 2 and 4 are composition claims. Claims 5-8 are method of using claims. This is the first action on the merits. The application concerns some 3-pyrimidin-4-yl-6,7-dihydro-5H-pyrazolo[1,2-a]pyrazol-1-one compounds, compositions, and uses thereof.

Priority

2. The status of non-provisional parent application should also be included. Since the parent application has become a patent, please update the first line of the specification with the expression "now Patent No. 6,730,668" following the filing date of the parent application.

Inventorship

3. Receipt is acknowledged of the statement requesting that Djung, Natchus, and De be deleted as a named inventor, which was filed with the Continued Prosecution Application (CPA) on 9/12/03. The inventorship has been corrected as requested.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. the compound named in this claim is not the compound pictured in this claim.

5. Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The specification does not set forth any steps involved in determining how to identify "disease states affected by the level of extracellular inflammatory cytokines in humans". It is unclear what diseases and treatments applicant is intending to encompass. A list is given in lines 4-6, page 64. However, this list uses open language. Is this the complete list of diseases whose treatment is being claimed or are there others? Determining whether a given disease responds or does not respond to such a receptor antagonist and thus, covered by the claim language, will require extensive and potentially inconclusive clinical research. With out such clinical research to identify the patients and diseases Applicants intend to treat, the physician skilled in the clinical arts cannot determine the metes and bounds of the claim. Hence, the claims are indefinite.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating rheumatoid arthritis (RA), does not reasonably provide enablement for treating osteoarthritis, diabetes, or any other disease states. The specification does not enable any physician skilled in the art of medicine, to make the invention commensurate in scope with these claims. The how to make requirement of the enablement statute, when applied to process claims, refers to operability and how to make the claimed process work. "The factors to be considered [in making an enablement rejection] have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims", *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546. The four main issues are the lack of any correlation between clinical efficacy for osteoarthritis or diabetes treatment and Applicants' single *in vitro* assay, the complete lack of any biological data in the specification, the state of the prior art, and the breadth of the claims.

There is an *in vitro* assay, drawn to inhibition of TNFα release, described in the passage spanning line 26, page 64 to line 7, page 65 with no data. Applicants do not state and it is not recognized in the clinical arts this assay is correlated to clinical efficacy for the treatment of osteoarthritis, diabetes, or other claimed diseases. The state of the clinical arts in TNFα mediated diseases in 1997 is summarized by Black (Ann. Rep. Med. Chem.) in the final paragraph, page 248 as "it remains to be seen if small molecule antagonists *** can offer therapeutic advantages". Applicants' compounds are small molecules. The state of the clinical arts in 1999 is provided by Chantry (Emerging Drugs). This reference teaches in the first paragraph, page 5 and in the first paragraph, page 8 that RA and Crohn's are the only art-recognized uses of TNFα antagonists. The state of the art in 2000 is summarized by Illei (Current Opinion in Immunology) in the abstract as "anti-TNF therapy has made a major impact on the treatment of inflammatory arthritides (sic) and Crohn's disease".

The scope of the claims involves all of the thousands of compounds of claim 5 as well as the unknown number of diseases embraced by the term "disease states affected by the level of extracellular inflammatory cytokines in humans". Thus, the scope of claims is very broad.

MPEP §2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here and undue experimentation will be required to practice Applicants' invention.

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969). A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b). Effective January

1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1 and 3 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 33 of U.S. Patent No. 6,730,668. Although the conflicting claims are not identical, they are not patentably distinct from each other because these two compounds are also named in lines 39-40, column 63 and lines 17-19, column 64, of claim 33.

8. Claims 2 and 4 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 36 of U.S. Patent No. 6,730,668. Although the conflicting claims are not identical, they are not patentably distinct from each other because claim 36 of the parent patent is drawn to compositions of a generic formula embracing the two species of the present claims 2 and 4. The presence of these two species in claim 33 of the parent patent provides the "blaze marks" pointing to the two present species.

9. Claims 2 and 4 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 13 of copending Application No. 10/689,388. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compound of claim 2 is the first named compound in claim 13 of copending Application No.

10/689,388. The compound of claim 4 is the compound listed third from the bottom of page 77 of copending Application No. 10/689,388..

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

10. Information regarding the status of an application should be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free). Please direct general inquiries to the receptionist whose telephone number is (703) 308-1235.

11. Please direct any inquiry concerning this communication or earlier communications from the Examiner to Thomas C McKenzie, Ph. D. whose telephone number is (571) 272-0670. The FAX number for amendments is (571) 273-8300. The PTO presently encourages all applicants to communicate by FAX. The Examiner is available from 9:00am to 5:30pm, Monday through Friday. If

attempts to reach the Examiner by telephone are unsuccessful, please contact James O. Wilson, acting SPE of Art Unit 1624, at (571)-272-0661.

Thomas C. McKenzie, Ph.D.
Primary Examiner
Art Unit 1624
(571) 272-0670

TCMcK/me